



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكرو فيلم

# بسم الله الرحمن الرحيم



**MONA MAGHRABY**



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# شبكة المعلومات الجامعية التوثيق الإلكتروني والميكرو فيلم



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# جامعة عين شمس

## التوثيق الإلكتروني والميكروفيلم

### قسم

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علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



**MONA MAGHRABY**



# **Effects of Direct Acting Antivirals on Glomerular Filtration Rates and Neutrophil Gelatinase-Associated Lipocalin during the Treatment of Hepatitis C Patients**

Thesis

Submitted for Partial Fulfillment of M.D Degree  
in **Internal Medicine**

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# List of Abbreviations

Abb.	Full term
ADPKD .....	Autosomal dominant polycystic kidney disease
AIN .....	Acute interstitial nephritis
AKI .....	Acute kidney injury
ALT .....	Serum alanine aminotransferase
AST .....	Serum aspartate aminotransferase
ATN .....	Acute tubular necrosis
CKD .....	Chronic kidney disease
DAA's .....	Direct-acting antivirals
DAC .....	Daclatasvir
ELISA .....	Enzyme linked immunosorbent assay
FDA .....	Food and Drug Administration
Fe .....	Iron
FGN .....	Fibrillary glomerulonephritis
FSGS .....	Focal segmental glomerulosclerosis
HCC .....	Hepatocellular carcinoma
HCV .....	Hepatitis C virus
HIV .....	Human immunodeficiency virus
HRS .....	Hepatorenal Syndrome
IFN .....	Interferon
Ig .....	Immunoglobulins
IgA .....	Immunoglobulin A
IgG .....	Immunoglobulin G
IQR .....	Interquartile range
IRS .....	Insulin receptor substrate proteins
ITGN.....	Immunotactoid glomerulonephritis
LRP2.....	Lipoprotein receptor-related protein 2
MAP .....	Mitogen activated protein kinase
MI .....	Myocardial infarction
MMP-9.....	Matrix metalloproteinase 9
MN.....	Membranous glomerulonephritis
MPGN .....	Membranoproliferative glomerulonephritis
MSFI .....	Migration stimulating factor inhibitor

# List of Abbreviations cont...

Abb.	Full term
NGAL .....	Neutrophil gelatinase associated lipocalin
NNPIs .....	Non-nucleoside polymerase inhibitors
NPIs .....	Nucleoside polymerase inhibitors
NS .....	Nonstructural proteins
PAN .....	Polyarteritis Nodosa
peg-IFN .....	Pegylated interferon
PIs .....	Protease inhibitors
RBP .....	Retinol binding protein
RBV .....	Ribavirin
RF .....	Rheumatoid factor
ROC Curve .....	Receiver Operating Characteristic Curve
SCR .....	Structurally conserved regions
SD .....	Standard deviation
SOF .....	Sofosbuvir
SPSS .....	Statistical package for Social Science
SR-B1.....	Scavenger receptor B1
SVR .....	Sustained viral response
TAPA-1.....	Target of anitproliferative antibody 1
TGFβ .....	Transforming Growth factor Beta
TLR .....	Toll-like receptors
TLR-2.....	Toll-like receptors
TLR-3.....	Toll-like receptors
TNF-α .....	Tumor Necrosis Factor alpha
VEGF .....	Vascular endothelial growth factor
WHO .....	World Health Organization

## INTRODUCTION

**H**epatitis C virus (HCV) infection is a major global health challenge, according to the World Health Organization (WHO) report in 2017, it is estimated that about 71 million people are chronically infected worldwide (*World Health Organization, 2017*).

Unfortunately, Egypt has one of the highest global burdens of hepatitis C virus (predominantly genotype 4) infections, it is estimated that prevalence of HCV is around 4.5% to 6.7% (*Doss et al., 2018*).

The ultimate goal of hepatitis C treatment is to reduce the occurrence of end-stage liver disease and its complications, including decompensated cirrhosis, liver transplantation, and Hepatocellular carcinoma (HCC). Initially, chronic hepatitis C was treated by conventional interferon (IFN) monotherapy which yielded very poor response rates. Addition of the guanosine analogue, ribavirin (RBV) to conventional IFN was associated with a slight improvement in sustained viral response (SVR) (*Suda and Sakamoto, 2015*).

The year 2011 marked the dawn of the new era of direct-acting antivirals (DAAs) for hepatitis C. DAAs were initially introduced as add-ons to the previous standard of care consisting of PEG-IFN $\alpha$ /RBV. In 2014, a breakthrough in HCV therapy was achieved with the introduction of IFN-free -oral

DAAs, with SVR rates in excess of 90% after 12 weeks of therapy (***Kamal, 2018***).

Concerns on renal safety may represent a limitation to a wide use of DAAs in HCV patients, despite the proven efficacy of this class of drugs. Furthermore, the reported unreliability of conventional markers of renal function in patients with liver cirrhosis can contribute to discourage DAA prescription (***Levin et al., 2013***).

HCV infection is prevalent in patients with renal impairment, diverse groups of patients with renal disease require consideration when treatment of hepatitis C is indicated. These include patients with chronic kidney disease (CKD) stage 4 (eGFR = 15–29 ml/min/1.73 m<sup>2</sup>) or those with CKD stage 5 (eGFR <15 ml/min/1.73 m<sup>2</sup>). Some of these groups, renal function could potentially improve with antiviral treatment. However, organ recovery may be delayed or worsened in others (***European Association for the Study of the Liver, 2018***).

In patients with severe renal dysfunction (eGFR <30 ml/min/1.73 m<sup>2</sup>), the safety of sofosbuvir-based regimens has been questioned. A recommended regimen in HCV genotype 4 is the combination of ritonavir-boosted paritaprevir and ombitasvir for 12 weeks with daily ribavirin (200 mg/day) if the haemoglobin level is >10 g/dl at (Baseline), or safer with

combination of grazoprevir and elbasvir for 12 weeks (*European Association for the Study of the Liver, 2018*).

Neutrophil gelatinase associated lipocalin (NGAL) is a novel kidney biomarker. It is a small glycoprotein secreted by epithelial cells (liver, kidney, lungs) and some white blood cells (neutrophils, monocytes and macrophages). It's filtered in the glomerulus and reabsorbed by the proximal tubules. It can be measured in blood and urine and so it is used as early marker of acute kidney injury (*Strazzulla et al., 2018*).